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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KAPUST, RACHEL B	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 02/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No.	Applicant(s)	
	09/977,577	MOESTRUP ET AL.	
	Examiner	Art Unit	
	Rachel B. Kapust	1647	

-- Th MAILING DATE of this communication appears on the cov r sheet with the correspondence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *1-18,28-31 and 36-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-27 and 32-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group III (encompassing claims 19-27 and 32-35) is acknowledged. The traversal is on the ground(s) that the claims of Group III are considered allowable, therefore Groups IV and V should be rejoined.

As stated in the previous office communication, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Any such process claims will be rejoined only after the product claims are found allowable, not before. Group III has not been found allowable, therefore the process claims of Groups IV and V are not rejoined at this time.

The restriction requirement is still deemed proper and is therefore made FINAL. Claims 1-18, 28-31, and 36-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions. Claims 19-27 and 32-35 are under consideration.

Information Disclosure Statement

The information disclosure statement filed April 22, 2003 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the document number 0041177 (Guyre *et al.*) is not identifiable. It is not identifiable because a) a copy of the document has not been submitted; b) the inventor of patent 41,177 is Harold *et al.*; and c) the document number is not a published application number. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Specification

The disclosure is objected to because of the following informalities:

The use of the trademarks SEPHAROSE™ (p. 33), BIACORE™ (p. 34), TRIZOL™ (p. 42), SUPERSCRIPT™ (p. 42), and ROBOCYCLER™ (p. 42) have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

On p. 39, lines 36 and 37, two PCR primer sequences are disclosed. However, they are not identified by their SEQ ID NO. Appropriate correction is required. MPEP § 2422.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 19-26 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 19-26 are drawn to CD163 variants, all of which are unaltered, naturally occurring articles. Thus, they are not articles of "manufacture". These rejections may be obviated by amending the claims to read "an isolated CD163 variant" or "a purified CD163 variant" so long as there is support for the amendment in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-27 and 32-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19-27 and 32-35 are drawn to CD163 "variants". The only definition provided for "CD163 variant" is found on page 21, and no structural limitations are provided for the variants. It is not clear to what degree proteins may vary from CD163 and still be considered a "variant". Thus, the metes and bounds of "variant" are unclear.

In addition, claim 22 is drawn to a CD163 variant comprising certain scavenger receptor cysteine-rich (SRCR) domains, or "a variant thereof". In other words, claim 22 is drawn to a variant of a variant, the metes and bounds of which are unclear. Claim 23 is rejected because it is dependent on claim 22.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-27 and 32-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention; 2) state of the prior art; 3) relative skill of those in the art; 4) level of predictability in the art; 5) existence of working examples; 6) breadth of claims; 7) amount of

direction or guidance by the inventor; and 8) quantity of experimentation needed to make and/or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claims 19-27 and 32-35 are drawn to CD163 variants. Applicants state that the term "CD163 variant" is meant to include functional equivalents of CD163, fragments of CD163, and amino acid sequences capable of being recognized by an antibody also capable of recognizing CD163 (p. 21, lines 11-18). Functional equivalents may be obtained by addition, substitution or deletion of at least one amino acid (p. 22). Applicants further teach that certain regions of CD163 are readily mutatable or capable of being completely deleted without having any significant effect on the binding activity of the resulting fragment (p. 26, lines 14-19).

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, such as various sites or regions directly involved in binding, activity, and in providing the correct three-dimensional spatial orientation of binding and active sites.

However, Applicants have provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein that are tolerant to change and the nature and extent of changes that can be made in these positions. The specification provides no guidance as to which (if any) of the amino acids can be changed or deleted to yield a functional variant of CD163. Applicants have provided no guidance as to which amino acid residues are required for binding to the Hp-Hb complex. Even if an active site or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues.

Due to the large quantity of experimentation necessary to generate the infinite number of proteins recited in the claims and screen the same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide

activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Claims 27 and 32-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, were it enabling for a medicament comprising CD163 or a diagnostic composition comprising CD163, would still not reasonably provide enablement for medicaments comprising all variants of CD163 or diagnostic compositions comprising all variants of CD163. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 27 and 32-34 are drawn to medicaments comprising CD163 variants and diagnostic compositions comprising CD163 variants. Applicants state that the term "CD163 variant" is meant to include functional equivalents of CD163, fragments of CD163, and amino acid sequences capable of being recognized by an antibody also capable of recognizing CD163 (p. 21, lines 11-18). Functional equivalents may be obtained by addition, substitution or deletion of at least one amino acid (p. 22). Applicants further teach that certain regions of CD163 are readily mutatable or capable of being completely deleted without having any significant effect on the binding activity of the resulting fragment (p. 26, lines 14-19).

As stated above, certain positions in the amino acid sequence are critical to the protein's structure/function relationship, such as various sites or regions directly involved in binding, activity, and in providing the correct three-dimensional spatial orientation of binding and active sites. Applicants have not provided any guidance as to which amino acids can be substituted, deleted, or inserted while still encoding a functional CD163. Although Applicants teach that CD163 variants may be used in the treatment of haemolysis, Applicants have not provided examples of any such variants. Applicants have provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without

undue experimentation, the positions in the protein that are tolerant to change and the nature and extent of changes that can be made in these positions.

Due to the large quantity of experimentation necessary to generate the infinite number of proteins recited in the claims and screen the same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Claims 19-27 and 32-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are drawn to a genus, *i.e.* CD163 variants. Applicants have disclosed three species (Q07901, Q07900, and Q07899 on p. 21), but have not disclosed sufficient species for the broad genus of any amino acid sequence comprising a CD163 variant.

The instant disclosure of three CD163 variant amino acid sequences does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length genes and fragments of genes. A description of a genus of proteins may be achieved by means of a recitation of a representative number of proteins, defined by amino acid sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of proteins. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no

information regarding the relation of structure to function. Rather, applicants teach that certain regions of CD163 are readily mutatable or capable of being completely deleted without having any significant effect on the binding activity of the resulting fragment (p. 26, lines 14-19). Structural features that could distinguish the compounds in the genus from other scavenger receptor molecules are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the proteins encompassed: there is no guidance in the art as to what the defining characteristics of CD163 might be. Thus, no identifying characteristics or properties of the instant proteins are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, the disclosure of three CD163 variants is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19-27 and 32-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Law *et al.* (1993, *Eur. J. Immunol.* 23: 2320-2325, submitted by applicants July 5, 2002). Claims 19-26 are drawn to CD163 variants capable of binding at least one haptoglobin-hemoglobin (Hp-Hb) complex. Claims 27 and 32-35 are drawn to medicaments and compositions comprising CD163 variants. Law *et al.* teach the wild-type CD163 sequence (also known as M130) (GenBank accession number Z22968) and the sequences of three CD163 variants (GenBank accession numbers Z22969, Z22970, and Z22971). The ability to bind Hp-Hb complexes is an inherent feature of CD163 and the CD163 variants. Law *et al.* further teach that CD163 is found on all circulating monocytes and most tissue macrophages, and they teach monoclonal antibodies

useful for identifying CD163 and variants of CD163 (p. 2320). Thus, Law *et al.* anticipate claims 19-27 and 32-35.

Claims 19-26 and 32-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Högger *et al.* (1998, *J. Immunol.* 161: 1883-1890). The claims are as stated above. Högger *et al.* teach splice variants of CD163 (p. 1886, Figure 3). Högger *et al.* also teach that CD163 (also known as RM3/1) is expressed exclusively on human monocytes and macrophages, predominantly in the late phase of inflammatory processes (p. 1883, column 1). Therefore Högger *et al.* teach CD163 variants that are diagnostic of inflammatory reactions. Claims 19-26 and 32-35 are anticipated by Högger *et al.*

Conclusion

NO CLAIMS ARE ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel B. Kapust whose telephone number is (571) 272-0886. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

RBK
2/2/04

JANET ANDRES
PATENT EXAMINER